REMARKS

Favorable reconsideration is respectfully requested in view of the foregoing amendments and the following remarks.

Claims 7 and 24 have been rewritten as new claims 25 and 26 in independent form. Claim 9 has been amended so as to be dependent upon claim 24. New claim 27 is added corresponding to claim 9.

The objection to claims 7, 9 and 24 set forth in item 5 of the Action is deemed to be overcome by the foregoing amendments.

The disclosure has been amended to recite the Example number.

The objection to the disclosure set forth in item 6 is deemed to be overcome by the foregoing amendments.

Claims 25 and 26 are limited to a brain sample or CSF sample.

The rejection of claims 7, 9 and 24 under 35 USC 112, first paragraph, set forth in item 7 is deemed to be overcome by the foregoing amendments.

Claims 25 and 26 have been drafted according to the suggestions of the Examiner in item 8 of the Action.

The rejection of claims 7, 9 and 24 is deemed to be overcome by the foregoing amendments.

Claims 7, 9 and 24 are rejected under 35 USC 102 as anticipated by Vandermeeren et al. This ground of rejection is respectfully traversed as applied to the new and amended claims.

The Examiner states that use of the word "comprises" anywhere in the claim reciting SEQ ID NO: 2 opens the claim up to encompass the previous art of record which uses antibodies, including AT8, which was raised against a polypeptide "comprising" SEQ ID NO: 2.

However, AT8 is not considered raised against a partial peptide according to claims 25 and 26, because AT8 does not recognize a partial peptide in which a serine residue at position 199 is phosphorylated. Please refer to Figure 1B of the declaration filed on November 15, 2003. The antibody AT8 did not react with either peptide PS199 in which a serine residue at position 199 is

phosphorylated (Fig. 1B, lane 1a) or peptide PS199 PS202 in which serine residues at position 199 and 202 are simultaneously phosphorylated (Fig. 1B, lane 2c).

Therefore, the cited reference fails to disclose the methods according to claims 25 and 26, which require that the antibody must "specifically recognizing said phosphorylation site of said partial peptide", i.e. the phosphorylated a serine residue at position 199. See claims 25 and 26, steps (b).

Accordingly, the cited references fails to disclose the claimed methods.

Claims 7, 9 and 24 were also rejected under 35 USC 103 as being unpatentable over Sato et al. in view of Ishiguro et al. This ground of rejection is respectfully traversed as applied to the new and amended claims.

Sato discloses that paired helical filaments (PHFs) accumulate in the neuron of AD brain and highly phosphorylated tau protein was found to be a component of PHFs. Ishiguro discloses antibodies against SEQ ID NO: 2. However, both Sato and Ishiguro do not disclose a reactivity of the antibody with a brain or CSF sample of an individual having Alzheimer's disease.

The antibody used in the claimed method specifically recognizes a phosphorylated tau protein in individual having Alzheimer's disease. Please refer to Figs. 2 and 3 of this application. These drawings show reactivity of the SDS precipitation fraction of human brain extract obtained in Example 2 with various antibodies against phosphorylated partial peptides. Among the antibodies, for example, PS262, PS413 and PS422 reacted with normal brain extract (Fig. 2 lanes 6-10) as well as brain extract from patients having Alzheimer's disease. On the other hand PS199 did not react with normal brain extract while it reacted with brain extract of patients having Alzheimer's disease. Thus, not all antibodies can be used for detecting patients having Alzheimer's disease.

As explained above, antibodies against a partial peptide in which serine residue at position 199 is phosphorylated are remarkably useful for detecting Alzheimer's disease. This discovery could not have been expected from the prior art.

Accordingly, reconsideration and allowance is solicited.

Respectfully submitted,

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